

Abstract

The present invention relates to insoluble compositions containing acylated proteins selected from the group consisting of acylated insulin, acylated insulin analog, and acylated proinsulin, and formulations thereof. The formulations are suitable for parenteral delivery or other means of delivery, to a patient for extended control of blood glucose levels. More particularly, the present invention relates to compositions comprised of an acylated protein complexed with zinc, protamine, and a phenolic compound such that the resulting microcrystal is analogous to the neutral protamine Hagedorn (NPH) insulin crystal form. Surprisingly, it has been discovered that compositions of such acylated proteins have therapeutically superior subcutaneous release pharmacokinetics, and more extended and flatter glucodynamics, than presently available commercial preparations of NPH insulin. Yet, the present crystals retain certain advantageous properties of NPH crystals, being readily able to be resuspended and also mixable with soluble insulins.